Low Level of Vegetative State After Traumatic Brain Injury in a Swiss Academic Hospital

Stretti, Federica ; Klinzing, Stephanie ; Ehlers, Ulrike ; Steiger, Peter ; Schuepbach, Reto ; Krones, Tanja ; Brandi, Giovanna

Abstract: BACKGROUND:No standards exist regarding decision making for comatose patients, especially concerning life-saving treatments. The aim of this retrospective, single-center study was to analyze outcomes and the decision-making process at the end of life (EOL) in patients with traumatic brain injury (TBI) in a Swiss academic tertiary care hospital. METHODS:Consecutive admissions to the surgical intensive care unit (ICU) with stays of at least 48 hours between January 1, 2012 and June 30, 2015 in patients with moderate to severe TBI and with fatality within 6 months after trauma were included. Descriptive statistics were used. RESULTS:Of 994 ICU admissions with TBI in the study period, 182 had an initial Glasgow Coma Scale <13 and a length of stay in the ICU >48 hours. For 174 of them, a 6-month outcome assessment based on the Glasgow Outcome Scale (GOS) was available: 43.1% (36.0%-50.5%) had favorable outcomes (GOS 4 or 5), 28.7% (22.5%-35.9%) a severe disability (GOS 3), 0.6% (0%-3.2%) a vegetative state (GOS 2), and 27.6% (21.5%-34.7%) died (GOS 1). Among the GOS 1 individuals, 45 patients had a complete dataset (73% men; median age, 67 years; interquartile range, 43-79 years). Life-prolonging therapies were limited in 95.6% (85.2%-99.2%) of the cases after interdisciplinary prognostication and involvement of the surrogate decision maker (SDM) to respect the patient's documented or presumed will. In 97.7% (87.9%-99.9%) of the cases, a next of kin was the SDM and was involved in the EOL decision and process in 100% (96.3%-100.0%) of the cases. Written advance directives (ADs) were available for 14.0% (6.6%-27.3%) of the patients, and 34.9% (22.4%-49.8%) of the patients had shared their EOL will with relatives before trauma. In the other cases, each patient's presumed will was acknowledged after a meeting with the SDM and was binding for the EOL decision. CONCLUSIONS: At our institution, the majority of deaths after TBI follow a decision to limit life-prolonging therapies. The frequency of patients in vegetative state 6 months after TBI is lower than expected; this could be due to the high prevalence of limitation of life-prolonging therapies. EOL decision making follows a standardized process, based on patients' will documented in the ADs or on preferences assumed by the SDM. The prevalence of ADs was low and should be encouraged.

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Low Level of Vegetative State After Traumatic Brain Injury in a Swiss Academic Hospital

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BACKGROUND: No standards exist regarding decision making for comatose patients, especially concerning life-saving treatments. The aim of this retrospective, single-center study was to analyze outcomes and the decision-making process at the end of life (EOL) in patients with traumatic brain injury (TBI) in a Swiss academic tertiary care hospital.
METHODS: Consecutive admissions to the surgical intensive care unit (ICU) with stays of at least 48 hours between January 1, 2012 and June 30, 2015 in patients with moderate to severe TBI and with fatality within 6 months after trauma were included. Descriptive statistics were used.
RESULTS: Of 994 ICU admissions with TBI in the study period, 182 had an initial Glasgow Coma Scale <13 and a length of stay in the ICU >48 hours. For 174 of them, a 6-month outcome assessment based on the Glasgow Outcome Scale (GOS) was available: 43.1% (36.0%–50.5%) had favorable outcomes (GOS 4 or 5), 28.7% (22.5%–35.9%) a severe disability (GOS 3), 0.6% (0%–3.2%) a vegetative state (GOS 2), and 27.6% (21.5%–34.7%) died (GOS 1). Among the GOS 1 individuals, 45 patients had a complete dataset (73% men; median age, 67 years; interquartile range, 43–79 years). Life-prolonging therapies were limited in 95.6% (85.2%–99.2%) of the cases after interdisciplinary prognostication and involvement of the surrogate decision maker (SDM) to respect the patient's documented or presumed will. In 97.7% (87.9%–99.9%) of the cases, a next of kin was the SDM and was involved in the EOL decision and process in 100% (96.3%–100.0%) of the cases. Written advance directives (ADs) were available for 14.0% (6.6%–27.3%) of the patients, and 34.9% (22.4%–49.8%) of the patients had shared their EOL will with relatives before trauma. In the other cases, each patient's presumed will was acknowledged after a meeting with the SDM and was binding for the EOL decision.
CONCLUSIONS: At our institution, the majority of deaths after TBI follow a decision to limit life-prolonging therapies. The frequency of patients in vegetative state 6 months after TBI is lower than expected; this could be due to the high prevalence of limitation of life-prolonging therapies. EOL decision making follows a standardized process, based on patients' will documented in the ADs or on preferences assumed by the SDM. The prevalence of ADs was low and should be encouraged. (Anesth Analg 2018;127:698–703)

KEY POINTS

- **Question:** How is the outcome and the decision-making process at the end of life of patients with traumatic brain injury in a Swiss academic hospital?
- **Findings:** The frequency of patients in vegetative state 6 months after injury is negligible (0.6%), and nonsudden deaths after conscious end of life are frequent (96%), after a standardized process based on interdisciplinary prognostication and involvement of surrogate decision makers.
- **Meaning:** The high prevalence of decisions to limit life-sustaining therapies to respect the documented or assumed will of patients might have led to an earlier death among patients who are potentially in vegetative state.

Traumatic brain injury (TBI) is a sudden event and the leading cause of death and disability among young people. Up to 95% of patients with severe TBI die,[1] and 20% of the survivors experience a low quality of life.[2] Due to the neurological impairment, patients are incapable of giving informed consent and discussing therapeutic options. Clinicians involved in the care of TBI deal with many ethical challenges[3,4] such as determining appropriate treatment strategies for the patient during the vulnerable period in the intensive care unit (ICU), which might result in an unwanted futile outcome. Futile care is not defined by universally recognized, objective guidelines, but rather by the values of the patient, his or her family, and health care providers.[5,6]

Cultures, religions, and legislation[7–9] influence end-of-life (EOL) processes and the balance between ethical principles. No standards exist for decision making on treatment for comatose patients, especially concerning life-saving

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treatments.[10–12] In Europe and the United States, the prevailing ethical principles are respect for the patient's will and his or her autonomy.[13] In contrast, a more paternalistic approach is preferred by doctors and families in China.[14]

In Switzerland, the decision process is particular in 2 ways. First, the community delegates wide competence to the treating physicians in determining whether the patient's probable outcome is undesirable (ie, futile). For example, Swiss guidelines concerning life-sustaining treatments after resuscitation of adults[15] differ from other countries.[2] In cases of expected persistent high level of dependence, a limitation of life-prolonging therapies may be indicated if a life with severe disability would be contrary to the patient's will. Second, the law relating to the protection of adults[16] urges the treating physician to comply with the patient's presumed will. The law further prescribes that a surrogate decision maker (SDM) needs to be appointed, normally a family member. Discussion with the SDM will determine further therapeutic decisions, based on what he or she believes that patient's will would be. Accordingly, for patients unable to communicate, such as TBI patients, the SDM—and not the physician—decides on behalf of the patient.

Considering the intensity of the decision-making process for patients with TBI, the recent increased use of limitation of life-prolonging therapies in this specific population,[17] and the particularities of Swiss culture concerning the concept of futility and SDM, this study analyzes outcome and the EOL process of patients with moderate and severe TBI in a Swiss university hospital.

METHODS

This retrospective, single-center study was conducted in the surgical ICU of the University Hospital of Zurich, Switzerland, a tertiary care hospital, in accordance with Good Clinical Practice guidelines, the provisions of the Declaration of Helsinki, and the national legal and regulatory requirements. The Institutional Ethics Committee of Zurich (KEK-ZH-Nr. 2016-00332) approved this project and waived the need for informed consent of the participants or their legal representatives (data were entered in the database anonymously).

Inclusion Criteria

All adults (>15 years of age) with moderate to severe TBI (defined by a Glasgow Coma Scale [GCS] <13 before sedation and intubation) admitted to the ICU between January 1, 2012 and June 30, 2015 who died within 6 months after trauma were included. Similar to previous publications on this topic,[18,19] we decided to include both moderate and severe TBI patients, to have a larger cohort of patients without further extending the study period, to limit possible confounding factors in patient management.

Patients discharged from the ICU within 48 hours were excluded to prevent analyses of patients with initially overestimated severity[20] and no need of intensive treatment (eg, due to the influence of alcohol at the time of trauma, whose prevalence is high in our population[21]) and to exclude early sudden fatalities occurring before a meeting with the SDM was held. At our ICU, decisions to limit life-prolonging therapies are rarely taken within the first 48 hours, as recommended also for patients with intracranial hemorrhage.[22] A meeting between medical staff and relatives is set up within the first 48 hours from trauma to discuss the prognosis and the patient's will and to decide on a goal of care. This is based on the documented and assumed will of the patient and interdisciplinary prognostication, made by ICU doctors and nurses, neurologists, neurosurgeons, trauma surgeons, and ethics experts.

Data Collection

Subjects were retrospectively identified within the hospital's electronic database (KISIMTM, Cistec Zurich, Switzerland), and data were retrieved if the subject was diagnosed with TBI (ICD Code S00-S09). Medical charts were reviewed, and TBI severity was classified according to the first GCS before sedation and intubation. A GCS of 12–8 defines a moderate and a GCS <8 a severe TBI.

Long-term functional outcomes were assessed by 2 senior intensivists with experience in care of patients with TBI (S.K., U.E.). The Glasgow Outcome Scale (GOS) 6 months after trauma was assessed with a structured questionnaire. Age, sex, length of stay in the ICU, duration of mechanical ventilation expressed in days, place of death, and the modality of EOL decision were recorded. The EOL decision was categorized into:

1. Withholding of therapy: new or existing life-support therapy was not started or intensified (eg, cardiopulmonary resuscitation, intubation, and mechanical ventilation);
2. Withdrawal of therapy: active decision to stop or remove a life-sustaining treatment (eg, mechanical ventilation, high inspiratory fraction of oxygen, infusion of catecholamines);
3. Alleviation of pain and symptoms of agony: administration of sedatives (propofol or midazolam) and/or opiates at the time of death.

Other data collected were:

- Time of the EOL decision (number of days after trauma);
- Time to death (number of days after trauma);
- Time elapsed from EOL decision and patient's death (number of days);
- Presence of written advance directives (ADs) and/or information that patient discussed EOL issues with relatives before the trauma occurred;
- Initiator and people involved in EOL decisions (doctors, nurses, SDMs, legal guardians);
- Prognostic scores: Injury Severity Score, and its head-specific Abbreviated Injury Scale, severity of systemic derangements during the first 24 hours in the ICU, as measured by the Simplified Acute Physiologic Score II, and the International Mission for Prognosis and Analysis of Clinical Trials (IMPACT) score for prediction of mortality and unfavorable outcomes 6 months after TBI. The IMPACT score is based on age, clinical findings (GCS motor component, pupillary reactivity), computed tomographic characteristics, secondary insults (hypoxemia, hypotension), and laboratory values on admission (glucose, hemoglobin).

EOL Process at Our Institution

At our ICU, a meeting with the SDM is organized within 48 hours after ICU admission to explore plausible patient's will and attitude to life and the family's expectations. Reevaluations are repeated and SDMs are regularly informed. If a conflict arises between medical staff, family, and SDMs, an ethics expert is involved. As suggested by Geurts et al,[23] these meetings are led by the attending physician, who informs the others on disease, treatment options, and prognosis with and without treatment. A brief report concerning the content of these meetings is included in the electronic medical records.

In cases of patients with locked-in syndrome, as long as the possibility to communicate with the patient is maintained—even if merely limited to movements of the eyes—the patient should be involved in the decision process about goals of care. The SDM may confirm that the decision taken respects the patient's will. Due to the peculiarity of this disease pattern, the expertise of an ethics expert could help to manage the case.

Statistical Analysis

Normal distribution of data was analyzed by D'Agostino-Pearson omnibus normality test. For descriptive statistics, categorical variables were expressed as absolute numbers with percentages, normally distributed quantitative variables as means ± standard deviation, and nonnormally distributed variables as medians with interquartile ranges. For nonnormal distributed data, the calculation of confidence intervals (CIs) was based on the binomial distribution; for proportion, we used the Wilson-Brown method. Statistical analysis was performed with Prism 6.00 (GraphPad Software, San Diego, CA).

Due to the retrospective nature of the study, the number of patients available was given. A sample size of 48 from a population of 10,000 produced a 2-sided 95% CI with a precision of 0.1197, when the actual proportion is near 0.2500. Precision computation was performed with PASS 15 (Kaysville, UT).

RESULTS

During the study period, 994 patients with TBI were consecutively admitted to the ICU (Figure 1). Of these, 182 had an initial GCS <13 and length of stay in the ICU of >48 hours. Eight individuals were excluded because of a missing 6-month GOS. For the remaining 174 individuals, the GOS distribution was analyzed (Figure 2): 43.1% (36.0%–50.5%; n = 75) had favorable outcomes (GOS 4 or 5), 28.7% (22.5%–35.9%; n = 50) showed severe disability (GOS 3), 0.6% (0%–3.2%; n = 1) remained in a vegetative state (GOS 2), and 27.6% (21.5%–34.7%; n = 48) succumbed to their injuries (GOS 1). No cases of locked-in syndrome were recorded. Among the GOS 1 individuals, 45 patients had a complete dataset and fulfilled the inclusion criteria of the study.

Ninety-six percent of these patients (85.2%–99.2%) (N = 43) died in the hospital, and 4% (0.8%–14.8%) died in a rehabilitation clinic. Demographic data and prognostic scores are shown in Table 1.

Decision-Making Process

In the GOS 1 population (N = 45), an EOL decision was taken in 95.6% (85.2%–99.2%) (n = 43) of the cases (Table 2).

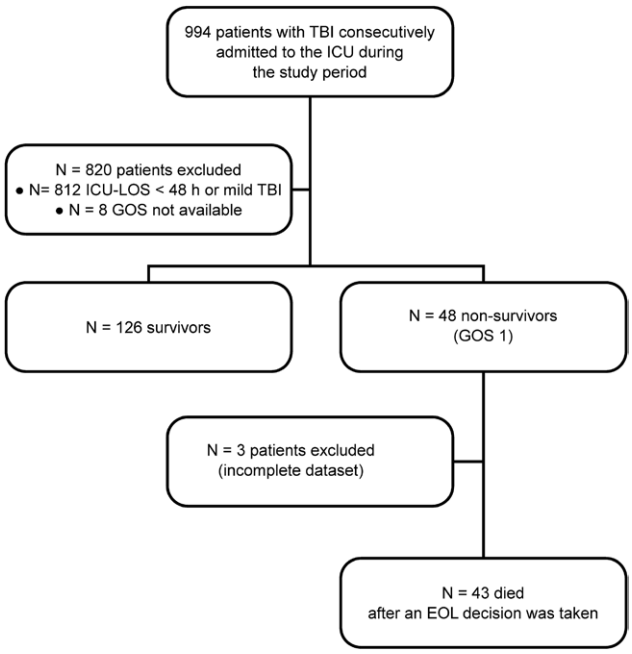

Figure 1. Description of the study population. EOL indicates end-of-life; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; LOS-ICU, length of stay in the intensive care unit; TBI, traumatic brain injury.

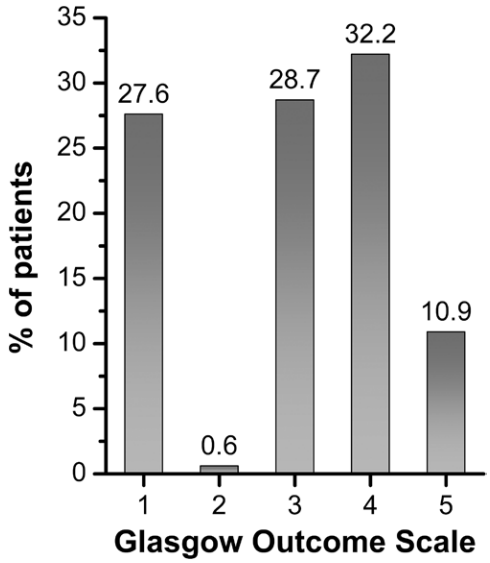

Figure 2. Six-month Glasgow Outcome Scale distribution. N = 174 patients. Glasgow Outcome Scale 1: death; Glasgow Outcome Scale 2: vegetative state; Glasgow Outcome Scale 3: severe disability; Glasgow Outcome Scale 4: moderate disability; Glasgow Outcome Scale 5: good recovery.

Written ADs were available for 14% (6.6%–27.3%) of patients, and an EOL conversation had been conducted with relatives before trauma in 34.9% (22.4%–49.8%) of the cases (in 5 of these cases, written ADs were available). The SDM was involved in the EOL process in all cases (96.3%, 100%). In 98% (87.9%–99.9%) of cases, a next of kin was the SDM. A legal guardian was appointed by Swiss authorities for 1 elderly patient without relatives (2.3%, 95% CI, 87.9%–99.9%).

Table 1. Demographic and Baseline Data (N = 45 Patients)

Variable	Value
Age (y, median)	67 (43–79)
Male (%)	73
LOS-ICU (d, median)	7 (4–11)
MV-days (d, median)	6 (3–9)
First GCS (median)	6 (3–9)
First GCSm (median)	3 (1–5)
ISS (mean)	28 ± 12
AIS head (median)	4 (3–4)
SAPS II (mean)	54 ± 13
IMPACT mortality (%, mean)	51 ± 18
IMPACT unfavorable outcome (%, median)	76 (62–85)

Data are expressed as mean ± SD, median and IQR, or frequency (%) as appropriate.

Abbreviations: AIS head, Abbreviated Injury Scale score referring to the head region; GCS, Glasgow Coma Scale; GCSm, motor component of the GCS; IMPACT mortality, probability of mortality 6 mo after traumatic brain injury based on IMPACT prognostic model; IMPACT unfavorable outcome, probability of unfavorable outcome 6 mo after traumatic brain injury based on IMPACT prognostic model; ISS, Injury Severity Score; LOS-ICU, length of stay in the intensive care unit; MV-days, number of days on mechanical ventilation; SAPS II, Simplified Acute Physiologic Score II during the first 24 h at the intensive care unit.

Table 2. Decision-Making Process Data (N = 43 Patients)

Data	Mean % (95% CI)
Trigger for the end-of-life discussion	
Doctors	85.7 (72.2%–93.3%)
Family	14.3 (6.7%–27.8%)
People involved in the end-of-life discussion	
Doctors	100.0 (91.8%–100.0%)
Nurses	78.9 (637%–88.9%)
Relatives	97.7 (87.9%–99.9%)
Ethics experts	2.3 (0.1%–12.1%)
Legal guardians	2.3 (0.1%–12.3%)
Surrogate decision maker	
Relatives	97.7 (87.9%–99.9%)
Ethics experts	2.3 (0.1%–12.1%)
Presence of written advance directives	14.0 (6.6%–27.3%)
End-of-life issues discussed with relatives before traumatic brain injury	34.9 (22.4%–49.8%)

Abbreviation: CI, confidence interval.

The EOL decision was initiated by doctors in 85.7% (72.2%–93.3%) of the cases. Doctors, nurses, and relatives were involved in the process (Table 2). In only 1 case did a conflict arise between family and physicians, and ethics and law experts were involved to solve it. No decision occurred without the presence of a SDM.

New goals of care after an EOL decision and discussion of palliative care modalities with the SDM are provided in Table 3.

DISCUSSION

In patients with moderate or severe TBI, we observed a negligible rate of 0.6% (0%–3.2%) of vegetative state at 6 months after injury. This may be due to the high rate of deaths after conscious EOL decisions (95.6%, 95% CI, 85.2%–99.2%) after interdisciplinary prognostication and involvement of the SDM to respect the documented or assumed patient's will.

Table 3. Data About End-of-Life Decision (N = 43 Patients)

Data	Mean % (95% CI)	Median Days (IQR)
Withdrawal of life-prolonging therapies	83.7 (70.0%–91.9%)	
Withholding of life-prolonging therapies	46.5 (32.5%–61.1%)	
Alleviation of symptoms with sedatives/opiates	97.7 (87.9%–99.9%)	
Time from traumatic brain injury to end-of-life decision		7 (4–14)
Time from traumatic brain injury to death		9 (6–15)
Time from end-of-life decision to death		1 (0–3)

Abbreviations: CI, confidence interval; IQR, interquartile range.

Outcome Futility

The rate of unfavorable outcomes (GOS 1–3) 6 months after TBI in our population was comparable to that found in the database[24] used to create the prognostic model IMPACT. Interestingly, we observed a negligible rate of vegetative state (GOS 2; 0.6%, 95% CI, 0%–3.2%), lower than that in cohorts from earlier reports. For example, the rate of vegetative state was higher in the Eurotherm trial[25] (8% in the hypothermia group and 17% in the normothermia group) and in the DEcompressive CRAniectomy (DECRA) trial[26] (12% in the decompressive craniectomy group and 2% in the control group).

Turgeon et al[27] reported deaths after limitation of life-sustaining therapies in 45%–87% of patients with TBI. In our population, this rate was higher, which might have led to an earlier death among patients who might potentially have become vegetative state cases.

The decision to limit life-sustaining therapies was based on the assumption that these would result in an unwanted outcome, in not respecting the patient's will, or in a futile outcome considered inappropriate by physicians.[28] Futility as a concept is neither objective nor universally recognized. However, for our purposes, quantitative futility means that a proposed therapy is unlikely to achieve the desired effect. On the other hand, qualitative futility means that a therapeutic action, even if successful, will result in a nondesired outcome[29]: futility is goal specific and based on a subjective evaluation of whether the goal of the intervention is futile. In our study, as assessed by ADs and the patients' assumed will, most individuals perceive persistent vegetative state and severe disability as undesirable and, thus, as futile outcomes, resulting in redirection of therapy and the patient's death, because the legal framework bases therapies on the patient's will. Consequently, patients who would otherwise have survived, although potentially remaining in vegetative state, passed away. This could explain why we observed a higher proportion of GOS1 cases than predicted by prognostic scores but a lower proportion of GOS2 cases.

The EOL Decision Process

Compared to other articles on EOL decisions after TBI,[30,31] our ICU is a late decision center: EOL decisions were taken on average 7 days after TBI, similar to the timing reported in a recent article referring to patients with intracranial hemorrhage.[32] We think that this period of aggressive treatment

before redirection of care permits adequate observation of the evolution of the damage to better define prognosis.

In 85.7% (72.2%–93.3%) of cases, physicians triggered the decision to limit life-prolonging therapies. There is room for discussion about whether this slightly paternalistic approach is justified; however, physicians could lead well-considered discussions based on the prognosis and the patient's values, as depicted by the SDM, or on his or her will as expressed in the AD. Relatives, when available, always participated in the EOL decision for their loved one. The content of these discussions was always reported in the medical records, in contrast to a previous study,[33] which highlighted scarce documentation of these discussions.

ADs: Medical Representative

The Swiss law relating to the protection of adults is based on the patient's autonomy: individuals have the right to make decisions based on their personal values and/or concepts. Written ADs, if available, are legally binding on the physician.

In our population, ADs (14.0%, 95% CI, 6.6%–27.3%) and discussions about EOL issues with relatives before trauma (34.9%, 95% CI, 22.4%–49.8%) were rare, as was also found in a recent paper performed in a Norwegian center.[31] This is probably due to the sudden nature of TBI[34] and the relative young age of the study population. Older patients with chronic illnesses are more likely to face the topic.[35,36] Nevertheless, the prevalence of ADs in Swiss terminal cancer patients remains low (29%),[37] revealing the lack of advance care planning concepts in Switzerland. This is different from other countries,[38,39] where discussions about advance care planning are part of routine health care.

In most cases, patients did not give any instruction, and a SDM granted consent to medical interventions based on the patient's presumed will. Because TBI often occurs suddenly and without warning, we recommend that even young people develop ADs and share them with their families; starting advance care planning early may help to alleviate some of the stress felt by relatives who are burdened by making EOL decisions.[40]

However, limitations of advance care planning must be considered. The drawing up of ADs requires engagement with death. In healthy phases of life, it is nearly possible to transpose oneself into the situation of a serious illness, and it is hard to imagine in advance which medical measures one would accept in extreme situations. Moreover, the degree of disability that patients can bear is higher than what they expected before the injury (disability paradox).[23]

Limitations

Our conclusions are limited by the study's retrospective nature and by the fact that it is a single-center study and consequently not representative of the country as a whole. Moreover, we collected data only on patients with TBI (GOS 1) who died within 6 months of their injury and, therefore, do not know if EOL decisions were taken even for patients who survived.

CONCLUSIONS

At our ICU, EOL decisions in patients with moderate or severe TBI are made frequently after interdisciplinary prognostication and involvement of the SDM. A possible consequence of this high rate of conscious EOL decisions followed by limitation of life-prolonging therapies is a negligible rate of patients in vegetative state compared to findings from previous studies. EOL decision making is challenging for both SDMs and health care professionals. Due to the sudden nature of TBI, we recommend that even young people write down ADs: starting advance care planning early could alleviate the stress felt by relatives burdened by decision making. Furthermore, we recommend a shared decision-making process: even if physicians initiate the discussion, representatives must be involved and the patient's will must be considered.

It would be interesting to conduct a multicenter study in different countries to analyze the differences in EOL processes in TBI patients and if/how these differences affect the outcome of this vulnerable group of patients. ■

DISCLOSURES

Name: Federica Stretti, MD.
Contribution: This author helped in the conception and design of the study; the acquisition, analysis, and interpretation of data; in drafting the study and revising it critically for key content.
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Contribution: This author helped in the conception and design of the study, the acquisition of data, in drafting the study and revising it critically for key content.
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Name: Giovanna Brandi, MD.
Contribution: This author helped in the conception and design of the study, the acquisition, analysis and interpretation of data, in drafting the study and revising it critically for key content.
This manuscript was handled by: Richard P. Dutton, MD.

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